REMARKS

Claims 1-15 are pending in the present application.

Entry of the above amendments is earnestly solicited. An early and favorable first action on the merits is earnestly solicited.

In compliance with 37 C.F.R. §§ 1.821-1.825 the specification has been amended to properly reference the SEQ ID NOS: of the Sequence Listing. In further compliance with 37 C.F.R. §§ 1.821-1.825, Applicants request that the computer readable form of the Sequence Listing, submitted as file "1110-0235.app" in the parent application no. 09/297,328, be transferred to the present application.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By_____
Gerald M. Murphy, Jr., #28,977

MaryAnne Armstrong, PhD., #40,069

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

GMM/MAA/csp
1110-0307P
Attachments

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning on page 12, line 15, has been amended as follows:

FIG. 1 is a view showing sequences of cDNA (SEQ ID NO:1) and translated amino acid (SEQ ID NO:2) for the variable region in the light chin of mouse F919-9-18 antibody. CDRs are underlined, and the first amino acid in the mature chain is underlined in duplicate.

The paragraph beginning on page 12, line 19, has been amended as follows:

FIG. 2 is a view showing sequences of cDNA (SEQ ID NO:3) and translated amino acid (SEQ ID NO:4) for the variable region in the heavy chain of mouse F919-9-18 antibody. CDRs are underlined, and the first amino acid in the mature chain is underlined in duplicate.

The paragraph beginning on page 12, line 23, has been amended as follows:

FIG. 3 is a view showing sequences of cDNA (SEQ ID NO:5) and translated amino acid (SEQ ID NO:6) for the variable region in the light chain of humanized F919 antibody. CDRs are underlined, and

the first amino acid in the mature chain is underlined in duplicate.

The paragraph beginning on page 13, line 2, has been amended as follows:

FIG. 4 is a view showing sequences of cDNA (SEQ ID NO:7) and translated amino acid (SEQ ID NO:8) for the variable region in the heavy chain of humanized F919 antibody. CDRs are underlined, and the first amino acid in the mature chain is underlined in duplicate.

The paragraph beginning on page 13, line 6, has been amended as follows:

FIG. 5 is a view showing the nucleotide sequence (SEQ ID NO:9) and the amino acid sequence (SEQ ID NO:10) deduced therefrom of a part of a vector (pM1304) containing the nucleotide sequence of the cDNA coding for the shFas(nd29)-Fc which is a Fas derivative (to 64th amino acid (to 275th DNA)).

The paragraph beginning on page 13, line 11, has been amended as follows:

FIG. 6 is a view showing the nucleotide sequence (SEQ ID NO:9) and the amino acid sequence (SEQ ID NO:10) deduced therefrom of a part of the vector (pM1304) containing the nucleotide sequence of the cDNA coding for the shFas(nd29)-Fc which is a Fas derivative

(from 65th amino acid to 144th amino acid (from 276th DNA to 515th DNA)). Possible N-glycosylation sites are marked with *.

The paragraph beginning on page 13, line 17, has been amended as follows:

FIG. 7 is a view showing the nucleotide sequence (SEQ ID NO:9) and the amino acid sequence (SEQ ID NO:10) deduced therefrom of a part of the vector (pM1304) containing the nucleotide sequence of the cDNA coding for the shFas(nd29)-Fc which is a Fas derivative (from 145th amino acid to 224th amino acid (from 516th DNA to 755th DNA)). Possible N-glycosylation site is marked with *.

The paragraph beginning on page 13, line 23, has been amended as follows:

FIG. 8 is a view showing the nucleotide sequence (SEQ ID NO:9) and the amino acid sequence (SEQ ID NO:10) deduced therefrom of a part of the vector (pM1304) containing the nucleotide sequence of the cDNA coding for the shFas(nd29)-Fc which is a Fas derivative (from 225th amino acid to 304th amino acid (from 756th DNA to 995th DNA)).

The paragraph beginning on page 14, line 2, has been amended as follows:

FIG. 9 is a view showing the nucleotide sequence (SEQ ID NO:9) and the amino acid sequence (SEQ ID NO:10) deduced therefrom of a part of the vector (pM1304) containing the nucleotide sequence of the cDNA coding for the shFas(nd29)-Fc which is a Fas derivative (from 305th amino acid (from 996th DNA)).

The paragraph beginning on page 14, line 7, has been amended as follows:

FIG. 10 is a view showing the nucleotide sequence (SEQ ID NO:11) and the amino acid sequence (SEQ ID NO:12) deduced therefrom of a part of a vector (pM1317) containing the nucleotide sequence of the cDNA coding for the shFas(nd29)-hinge which is a Fas derivative (to 64th amino acid (to 275th DNA)).

The paragraph beginning on page 14, line 12, has been amended as follows:

FIG. 11 is a view showing the nucleotide sequence (SEQ ID NO:11) and the amino acid sequence (SEQ ID NO:12) deduced therefrom of a part of the vector (pM1317) containing the nucleotide sequence of the cDNA coding for the shFas(nd29)-hinge which is a Fas derivative (from 65th amino acid (from 276th DNA to 515th DNA)). Possible N-glycosylation sites are marked with *.

The paragraph beginning on page 14, line 18, has been amended as follows:

FIG. 12 is a view showing the nucleotide sequence (SEQ ID NO:11) and the amino acid sequence (SEQ ID NO:12) deduced therefrom of a part of the vector (pM1317) containing the nucleotide sequence of the cDNA coding for the shFas(nd29)-hinge which is a Fas derivative (from 516th DNA).

The paragraph beginning on page 23, line 8, has been amended as follows:

Among these, an example of the most preferable anti-Fas ligand antibody is mouse F919-9-18 antibody produced by hybridoma F919-9-18 which was originally deposited on June 22, 1995 in National Institute of Bioscience and Human Technology, Agency of Industrial Science and Technology (1-3, Higashi 1-chome, Tsukuba-shi, Ibaraki-ken, Japan) (Accession No. P-15002) and transferred from the original deposition to the international deposition on May 9, 1996 (Accession No. FERM BP-5535). The sequences of the variable regions of the antibody are shown in FIG. 1 (cDNA is described in ~~SEQ. ID No. 1~~ SEQ ID NO:1) and FIG. 2 (cDNA is described in ~~SEQ. ID No. 2~~ SEQ ID NO:3).

The paragraph beginning on page 27, line 17, has been amended as follows:

More preferably, the anti-Fas ligand antibody used in the present invention is a reshaped human antibody wherein complementarity determining region (CDR) of the human antibody is replaced with the complementarity determining region derived from the antibody of a mammal other than human such as mouse. More illustratively, the constant region and the framework region are preferably of human origin, and the complementarity determining region is preferably of non-human origin. A preferable example of the resahped human antibody (humanized antibody) is humanized antibody having the CDR derived from the mouse F919-9-18 antibody, which is disclosed in International Patent Application Publication No. WO 97/02290 (Application No. PCT/JP96/01820). Examples of the variable regions is shown in FIG. 3 (cDNA is described in ~~SEQ. ID No.3~~ SEQ ID NO:5) and FIG. 4 (cDNA is described in ~~SEQ. ID No. 4~~ SEQ ID NO:7).

The paragraph beginning on page 29, line 8, has been amended as follows:

Exemplary Fas derivatives are the extracellular domain of a

known Fas; a Fas antigen from which the transmembrane domain has been deleted; a chimeric protein of the extracellular domain of a Fas and another protein such as hFas-Fc which is a chimeric protein of the extracellular domain of human Fas and Fc fragment of human immunoglobulin. The Fas derivative may be the one prepared by any production process by utilizing known Fas sequences and known gene engineering techniques. For example, the process for producing the human Fas-Fc is described in the Examples of International Patent Application Publication No. WO 95/13293. Another preferable Fas derivative is the Fas having a deletion in its N terminal. A Fas derivative coded in plasmids (pM1304 and pM1317) included in the E. coli which were originally deposited on March 14, 1996 in National Institute of Bioscience and Human Technology, Agency of Industrial Science and Technology (1-3, Higashi 1-chome, Tsukuba-shi, Ibaraki-ken, Japan) (Accession Nos. P-15514 and P-15515) and transferred from the original deposition to the international deposition on March 6, 1997 (Accession No. FERM BP-5854 and Accession No. FERM BP-5855) (The accession Nos. in Taiwan were CCRC 940171 and CCRC 940170, respectively.) is a derivative including the extracellular domain of the known human Fas from which N terminal sequence of from 1st to 29th amino acid has been deleted, and this highly active derivative is a preferable example of the effective component for the prophylactic/therapeutic agent of the present invention (partial

nucleotide sequences in the vector (pM1304) including the nucleotide sequence of the cDNA coding for shFas(nd29)-Fc are described in FIGS. 5 to 9 and ~~SEQ No. 5~~ SEQ ID NO:9; and; partial nucleotide sequences in the vector (pM1317) including the nucleotide sequence of the cDNA coding for shFas(nd29)-hinge are described in FIGS. 10 to 12 and ~~SEQ No. 6~~ SEQ ID NO:11). The Fas derivatives used in the present invention as described above may be confirmed for their binding activity with the Fas ligand or inhibitory activity for the Fas-mediated apoptosis by an appropriate assay procedure.